High Impact Paper of the Month
December 2014

A rare variant in APOC3 is associated with plasma triglyceride and VLDL levels in Europeans.

Timpson, N. J., Walter, K., Min, J. L.,… & Soranzo, N., 2014.
Nature Communications, 5:4871

Paper commentary

In this high-profile research collaboration reported in Nature Communications last month, KASP genotyping was used to validate a genotyping-by-sequencing screen of genetic variation across a population which identified a rare variant (rs138326449-A minor allele frequency ~0.25% (UK) of the *APOC3* locus that is associated with lowered levels of circulating triglyceride.

Highlights of the paper

- Example of a rare, large effect variant identified at a population scale.
- Functional validation and analysis of the rare SNP variant effect.
- KASP genotyping and validation of a minor allele frequency SNP with 100% accuracy and concordance with genotypes from the whole-genome data set.
- Large study sample – KASP produced 100% accuracy over 10,145 cohort samples including 38 carriers of the rare allele.

Commentary

Elevated blood lipid levels are one of the major genetic factors predisposing a person to coronary artery disease. Currently, 40-60% of the variability in lipid levels is attributed to unknown heritable genetic factors. Although genome-wide studies have investigated and identified common variants that contribute to lipid levels, these only account for 10-12% of that heritability. Whole-genome sequencing projects conducted on well-phenotyped populations offer a genuine move forward for identifying variants that may account for the unexplained heritability.

Other articles you may be interested in

LDL-c-linked SNPs are associated with LDL-c and myocardial infarction despite lipid-lowering therapy in patients with established vascular disease..

Tragante, V., Doevendans, P.A., Nathoe, H.M.,… and Asselbergs, F.W., 2013. *European Heart Journal*, 34(37).

Presenting an approach to consider multiple genetic factors, researchers have here assigned a genetic risk score (GRS) for each sample based on the occurrence of 30 documented SNPs, and subsequently tested this for disease association.

The study used KASP genotyping in a fully blinded study of more than 8,000 samples. Highlighting the collective impact of multiple CAD/MI risk alleles, the GRS was found to correlate with both ischaemic stroke and peripheral artery disease.

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